Resolute℠

A Quick Reference Guide

A Phase 1/2 Investigational Gene Transfer Study for Late-Onset Pompe Disease in Adults

Why should I take part in a clinical study?

The decision to participate in a clinical study is personal. For many people it is an opportunity to get **medical care that is part of the study, receive an investigational product, or increase awareness and help the community** by contributing to medical research. Whatever the reason, participating in a clinical study is a unique opportunity to have access to investigational treatments and help research teams understand more about how investigational treatments work. Participation can help determine if investigational treatments are helpful, harmful, or no different than available options. The hope is to ultimately find treatments that are worthy of approval because they provide benefits that outweigh the risks.

What is the Resolute℠ clinical study for Pompe disease?

Resolute℠ is a clinical study of an investigational gene therapy (also referred to as gene transfer) called *SPK-3006*. It is being studied as a potential treatment for people diagnosed with late-onset Pompe disease (LOPD). To participate in this study, adults must be 18 years and older with clinically moderate LOPD receiving enzyme replacement therapy (ERT).

Each participant will receive a single intravenous (IV) infusion of *SPK-3006*, the investigational gene therapy, at either a low, middle, or high dose. Different doses are being studied with the goal of finding the lowest dose that may be safe and effective.

The goal of the study is to evaluate the safety and potential effectiveness of a single intravenous (IV) infusion of investigational *SPK-3006* in late-onset Pompe Disease (LOPD).

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What should I expect when participating?

Participating in a clinical study requires a variety of tests and you will be monitored throughout the study. Through these medical tests, the research team will learn how your body responds to the investigational gene therapy, the safety of the gene therapy, and how well the gene therapy may be working in your body.

There are 3 defined periods in the study:

1. **Screening period:** when participant eligibility is determined
2. **Dosing day:** a one-time IV infusion of investigational *SPK-3006*
3. **Follow-up:** physical and functional testing is conducted for about 52 weeks after receiving investigational *SPK-3006*

You will be carefully monitored throughout each phase of the study, and the results will be reviewed by the research team. The results will help the research team better understand the safety and potential impact of investigational *SPK-3006* on the overall health and quality of life of the study participants.

Why is Spark researching an investigational gene therapy to treat Pompe disease?

- Gene therapy is an investigational approach aimed at addressing the underlying genetic cause of late-onset Pompe disease (LOPD).
- Investigational *SPK-3006* contains a bioengineered *acid alpha-glucosidase enzyme (GAA)* gene that has the potential to continuously produce GAA enzyme. People with Pompe disease have missing or nonworking *GAA* genes, and this results in not enough GAA enzyme being made in their bodies. Without enough GAA enzyme, glycogen builds up, causing damage to certain tissues and organ systems. In LOPD this is most notable in muscles, leading to respiratory failure (difficulty breathing) and loss of motor function (difficulty moving).

SPK-3006 is an investigational gene therapy. It is not yet known if it is safe or effective in treating people with LOPD.

What kind of medical testing will be required?

Clinical studies are carefully designed with several considerations in mind, including the investigational treatment being studied, the medical condition the investigational treatment is being studied for, and the phase of the clinical study. The length of the clinical study and the ability to measure the potential impact are also important considerations.

Sometimes, it can seem that clinical studies include too many tests, tests that are repeated frequently, or tests that don't have a clear purpose. Remember, each test is included to help answer important research questions about the investigational treatment being studied:

- Is this investigational treatment safe?
- Is it doing what it is intended to do effectively?
- Are results changing over time?
- Is the effect of the investigational treatment measurable in a meaningful way?

All of the tests below are included in Resolute℠, as they will help the research team and study participants to better understand the overall impact of investigational *SPK-3006*.

Some types of tests performed	Why these tests are included in the study
Physical examinations, blood work, bodily fluid tests	To assess overall physical health and measure any changes over the course of the study to determine how the body (specifically, the liver and your lysosomes) processes *SPK-3006*
Muscle-function tests, such as the 6-minute walk test (6MWT)	To evaluate the strength and/or weakness of a group of muscles, how well the participant can tolerate a structured exercise test, and any changes in the ability to perform the test over time
Lung-function tests	To measure muscle strength and respiratory capacity as the participant breathes in and out, and any changes in the ability to perform the test over time
Quality of life questionnaires	To measure factors, such as activity level, pain, tiredness, mood, and health economic measurements (eg, missed school or work days)
Muscle biopsy (optional)*	To evaluate the health of muscle cells and assess enzyme activity and glycogen storage within muscle tissue

*A biopsy removes muscle tissue by making a small incision or by needle.

Visits with a physical exam must take place at a study site. All other assessments may be done by a home healthcare provider or at the study site at the choice of the investigator and the participant.

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Learn more about Resolute℠ by:

- Speaking with your healthcare professional
- Visiting **www.clinicaltrials.gov**
- Emailing **resolute@sparktx.com**

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